

What is claimed is:

1. A method of preventing binding of an anti-double stranded (ds)-DNA antibody to a neuron in a mammal exhibiting or at risk for lupus-induced cognitive dysfunction, wherein the
5 anti-ds-DNA antibody binds to an NR2 subunit of an NMDA receptor on the neuron, the method comprising treating the mammal with at least one peptide or mimetic in an amount effective to bind to the antibody, wherein the peptide or mimetic comprises an amino acid sequence of X1-Trp-X1-Tyr-X2, wherein X1 represents Asp or Glu, and X2 represents Gly or Ser.

10 2. The method of claim 1, wherein the peptide or mimetic comprises D-amino acids.

3. The method of claim 1, wherein the peptide or mimetic is 5-30 amino acids in length.

4. The method of claim 1, wherein the peptide or mimetic is 5-10 amino acids in length.

15 5. The method of claim 1, wherein the peptide or mimetic is 5 amino acids in length.

6. The method of claim 1, wherein the peptide or mimetic comprises Asp-Trp-Glu-Tyr-Ser.

20 7. The method of claim 1, wherein the mammal is a human.

8. The method of claim 1, wherein the effectiveness of the treatment is monitored using magnetic resonance spectroscopic imaging.

25 9. The method of claim 1, wherein the neuron is a hippocampal neuron.

10. A method of inhibiting progression of cognitive dysfunction in a mammal exhibiting or at risk for lupus-induced cognitive dysfunction, the method comprising treating the mammal
30 with at least one peptide or mimetic in an amount effective to bind to anti-ds-DNA antibodies that bind to an NR2 subunit of an NMDA receptor on a neuron, wherein the peptide or mimetic comprises an amino acid sequence of X1-Trp-X1-Tyr-X2, wherein X1 represents Asp or Glu, and X2 represents Gly or Ser.

35 11. The method of claim 10, wherein the peptide or mimetic comprises D-amino acids.

12. The method of claim 10, wherein the peptide or mimetic is 5-30 amino acids in length.

5 13. The method of claim 10, wherein the peptide or mimetic is 5-10 amino acids in length.

14. The method of claim 10, wherein the peptide or mimetic is 5 amino acids in length.

10 15. The method of claim 10, wherein the peptide or mimetic comprises Asp-Trp-Glu-Tyr-Ser.

16. The method of claim 10, wherein the mammal is a human.

15 17. The method of claim 10, wherein the neuron is a hippocampal neuron.

18. The method of claim 10, wherein the effectiveness of the treatment is monitored using magnetic resonance spectroscopic imaging.

20 19. The method of claim 10, wherein the effectiveness of the treatment is monitored using a behavioral test of hippocampal-dependent performance.

25 20. The method of claim 19, wherein the behavioral test of hippocampal-dependent performance is a memory test.

21. The method of claim 10, wherein the risk for lupus-induced cognitive dysfunction is determined by determining whether the mammal has anti-NR2 antibodies, wherein the presence of anti-NR2 antibodies indicates that the mammal is at risk for lupus-induced cognitive dysfunction.

30 22. The method of claim 21, wherein the cerebrospinal fluid is tested for the presence of anti-NR2 antibodies.

35 23. A method of inhibiting progression of cognitive dysfunction in a mammal exhibiting or at risk for lupus-induced cognitive dysfunction, the method comprising treating the brain of the

mammal with an agent that prevents binding of an anti-ds-DNA antibody to an NR2 subunit of an NMDA receptor of a neuron.

24. The method of claim 23, wherein the agent is an antibody or an aptamer that binds to
5 the NMDA receptor on a neuron but does not induce neuronal death.

25. The method of claim 23, wherein the neuron is in the hippocampus.

26. A method of inhibiting progression of cognitive dysfunction in a mammal exhibiting
10 or at risk for lupus-induced cognitive dysfunction, the method comprising treating the brain of the
mammal with an agent that inhibits death of a neuron that comprises a bound anti-ds-DNA
antibody on NR2 subunits of an NMDA receptor on the neuron.

27. The method of claim 26, wherein the hippocampus is treated.

15 28. The method of claim 26, wherein the agent reduces oxidative stress in the neuron.

29. The method of claim 26, wherein the agent increases glutathione levels in the neuron.

20 30. The method of claim 26, wherein the agent induces transcription factors that prevent
apoptosis of the neuron.

31. The method of claim 26, wherein the agent inhibits transcription factors that induce
25 apoptosis of the neuron.

32. The method of claim 26, wherein the agent increases aerobic glycolysis in
mitochondria of the neuron.

33. A method of inducing cognitive dysfunction in a nonhuman mammal, the method
30 comprising treating the mammal with a DNA mimotope in such a manner to induce antibodies
that bind to ds-DNA and an NR2 subunit of a neuron in the mammal, then, after the antibodies are
induced, treat the mammal to temporarily open the blood brain barrier.

34. The method of claim 33, wherein the DNA mimotope is an octamer on a polylysine backbone comprising the peptide or mimetic comprising the sequence X1-Trp-X1-Tyr-X2, wherein X1 represents Asp or Glu, and X2 represents Gly or Ser.

5 35. The method of claim 34, wherein the peptide or mimetic comprises the sequence Asp-Trp-Glu-Tyr-Ser.

36. The method of claim 34, wherein the peptide or mimetic consists of the sequence Asp-Trp-Glu-Tyr-Ser.

10 37. The method of claim 33, wherein the blood brain barrier is temporarily opened by treating the mammal with lipopolysaccharide.

38. The method of claim 33, wherein the mammal is a mouse.

15 39. A nonhuman mammal treated with a DNA mimotope in such a manner to induce antibodies that bind to ds-DNA and an NR2 subunit of a neuron in the mammal, then, after the antibodies are induced, treated to temporarily open the blood brain barrier.

20 40. The mammal of claim 39, wherein the DNA mimotope is an octamer on a polylysine backbone comprising the peptide or mimetic comprising the sequence X1-Trp-X1-Tyr-X2, wherein X1 represents Asp or Glu, and X2 represents Gly or Ser.

25 41. The mammal of claim 40, wherein the peptide or mimetic comprises the sequence Asp-Trp-Glu-Tyr-Ser.

42. The mammal of claim 40, wherein the peptide or mimetic consists of the sequence Asp-Trp-Glu-Tyr-Ser.

30 43. The mammal of claim 39, wherein the blood brain barrier is temporarily opened by treating the mammal with lipopolysaccharide.